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| 10/585,017 | 08/04/2008 | Jacob Bar-Tana | 1567/76581/JPW/CH | 7859 |

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| EXAMINER | |
|---|---|
| SZNAIDMAN, MARCOS L | |
| ART UNIT | PAPER NUMBER |
| 1628 | |
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| 11/10/2011 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/585,017 | BAR-TANA ET AL. | |
| | Examiner | Art Unit | |
| | MARCOS SZNAIDMAN | 1628 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 October 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5)☒ Claim(s) *11 and 23-31* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *11 and 23-31* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This office action is in response to applicant's reply filed on October 19, 2011.

### *Status of Claims*

Cancellation of claims 2-10, 12-19 and 22, and amendment of claims 11 and 24 is acknowledged.

Claims 11 and 23-31 are currently pending and are the subject of this office action.

Claims 11 and 23-31 are presently under examination.

The following species is under examination: Dyslipoproteinemia as the disease being treated.

### *Priority*

The present application is a 371 of PCT/IL04/001185 filed on 12/30/2004, and claims priority to provisional application No. 60/533,639 filed on 12/30/2003.

### *Rejections and/or Objections and Response to Arguments*

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not

Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 103 (Maintained Rejection)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11 and 23-31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Tana (US 4,689,344, cited in prior office action).

For claims 11, 23-24 and 30-31 Bar-Tana 1 teaches a method of treating hypercholesterolemia and hypertriglyceridemia (dyslipoproteinemia is a combined hypercholesterolemia and hypertriglyceridemia, see specification page, lines 14-15) in *Psamomys Obesus* (see column 20, line 65 through column 22, line 24, and more specifically table VI) comprising the administration of 3, 3, 14, 14 tetramethyl hexadecane 1, 16 dioic acid (MEDICA 16 or M16, see column 8, example 4). The animals were fed with "Amrod 935" Purina Chow diet supplemented with 0.1% of the active compound (see column 20, lines 65 through column 21, line 3). Bar-Tana further teaches that the daily dosage will depend on the age, needs and tolerance of the individual patient, but it will usually range from 50 mg to 5,000 mg per day (see column 7, lines 7-14).

Bar-Tana does not teach the dose ranges from about 100 mg per day to about 400 mg per day as disclosed in claim 11 or the dose range recited in claim 23 (200 mg per day to about 400 mg per day) and 30-31. However, the dosage taught by Bar-Tana

(50 to 5,000 mg daily, see above) clearly overlaps with the dosages of the instant claims (100 to 400 mg daily, 200 to 400 mg daily, 100 to 200 mg daily, and 200 mg). MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 11, 23-24 and 30-31 with a reasonable expectation of success.

For claims 25-29, Bar-Tana further teaches that the daily dosage of the compound of formula (I) will depend on the age, needs and tolerance of the individual patient (see column 7, lines 7-14).

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to further optimize the dose regimen based on age, tolerance and the individual needs of the patient as taught by Bar-Tana, thus resulting in the practice of claims 25-29 with a reasonable expectation of success.

*Response to Applicant's arguments related to the above rejection*

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that:

Bar-Tana does not teach that animal treatment of different component diseases of Syndrome X requires different dosages of M16.

Bar-Tana discloses that *Psamomys Obesus* (not humans) were fed "Amrod 935" Purina Chow diet supplemented with 0.1% of M16. See, Bar-Tana, column 20, lines 66-68. Table VI of Bar-Tana discloses that serum triglycerides and serum cholesterol levels were reduced in animals fed the M16 supplemented diet. Bar-Tana further discloses that feeding diabetic Psamomys Obesus a diet supplemented with 0.1% MI6 resulted in correction of the animals' glucose tolerance test curves. See, Bar-Tana, columns 21-22, Experiment II(c) and Table VIII. Moreover, the M16 supplemented diet lowered serum insulin levels in the diabetic animals. See, Bar-Tana, column 22, lines 13-16. Importantly, Bar-Tana does not disclose any data showing the effect of M16 administration at different doses. Thus, one of ordinary skill in the art at the time of applicants' invention would not have expected that any specific dosage of MI6 effective to treat one component disease of Syndrome X in a human would not be equally effective in treating other component diseases of Syndrome X. Consequently, one of ordinary skill in the art could not have predicted what dosages of M16 would be optimal for treating dyslipoproteinemia.

Examiner's response:

Bar-Tana teaches that at : "Psamomys Obesus were fed "Amrod 935" Purina Chow diet supplemented with 0.1% of compound M16 ad libitum (i.e. free-feeding), for periods of 80 or 140 days" (see column 20, line 66 through column 21, line 3). Bar-Tana further teaches formulations of M16 suitable for human administration like tablets, capsules, pills, etc., comprising different pharmaceutical carriers either for oral or parenteral administration (see column 6, line 54 through column 7, line 6). Finally, Bar-

Tana teaches that: The Pharmaceutical compositions according to the invention are preferably in dosage unit form, each unit containing from 50 to 500 mg of the active ingredient. The daily dosage according to the invention will depend on age, needs and tolerance of the individual patient, but will usually range from 50 mg to 5,000 mg per day" (see column 7, lines 7-15).

In summary, Bar-Tana teaches a dose regimen for monkeys and a dose regimen for humans for the treatment of dyslipoproteinemia among other diseases like diabetes, obesity etc. Even though Bar-Tana does not precisely teach the exact range that will be effective to treat each one of the above diseases individually; based on the teachings of Bar-Tana, the skilled in the art will be able to adjust the dose regimen based on individual needs (see Bar-Tana above), which means on the disease being treated (dyslipoproteinemia vs. obesity or diabetes), the age of the patient, tolerance, etc., which are routine practices in the pharmaceutical art, since the amount of a specific ingredient in a composition (in this case M16) is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize given the guidance of the prior art (see Bar-Tana guidance above). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of M16 needed to achieve the desired result in order to effectively treat dyslipoproteinemia based on the experimental data provided by bar-Tana for animals and humans, in particular when Bar-Tana already teaches a range of 50 to 5000 mg per day which overlaps with the instant claims. MPEP 2144.05 states: In the case where the claimed

ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

All this will result in the practice of the instant claims with a reasonable expectation of success.

Applicant argues that:

The previously submitted Declaration of Dr. Jacob Bar-Tana establishes that the maximal effective dose for reducing elevated triglycerides is 200 mg/day. For the Examiner's convenience, a copy of the Declaration submitted with the Amendment filed January 6, 2011 is attached hereto as Exhibit A. Specifically; doses of 30-200 mg/day decreased triglycerides by 42-53% from baseline, while dose escalation to 400 mg/day provided essentially the same decrease and did not produce any further significant decrease. See, Declaration, page 3 and Table I. In contrast, the data in Table 2 of the Declaration shows that a 200 mg/day dose of M16 (the maximal effective dose for lowering triglycerides) resulted in an insignificant increase in sensitization to insulin. See, page 5 and Table 2 of the Declaration. This result could not have been predicted from the teachings of Bar-Tana because Bar-Tana does not suggest a maximally effective dose for treating Syndrome X in a human, let alone a maximally effective dose of M16 for treating dyslipoproteinemia, a specific component disease of Syndrome X. As noted above, Bar-Tana discloses feeding M16 to Psamomys Obesus at a single concentration which was sufficient to reduce serum triglyceride, serum cholesterol, and

serum insulin levels, and to correct glucose tolerance test curves. Consequently, applicants' results which show that a different dosage of M16 is required to maximally treat different component diseases of Syndrome X in a human, in this case dyslipoproteinemia, is unexpected.

Examiner's response:

There is nothing unexpected with the fact that different dose ranges are required for different diseases (dyslipoproteinemia, obesity, diabetes, glucose tolerance, insulin sensitization, etc.). As discussed above, once the prior art teaches that these diseases can be treated with M16 within a certain dose range (50 to 5000 mg per day), and that the dose range will depend on the individual needs (i.e. type of disease being treated, age of patient, tolerance, etc.), it is then routine practice to optimize the dose range for each individual patient based on the specific disease being treated (like dyslipoproteinemia) and the general conditions of the patient. The discovery by Applicant that: "a dose range of 30-200 mg/day decreased triglycerides by 42-53% from baseline, while dose escalation to 400 mg/day provided essentially the same decrease and did not produce any further significant decrease" is nothing more than what will be expected from any drug: a strong dose/response correlation until the efficacy reaches its maximum (in this case 400 mg/day). Applicant's discoveries are no more than the result of routine optimization of parameters disclosed by the prior art (Bar-Tana).

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS L SZNAIDMAN/
Primary Examiner, Art Unit 1628
October 24, 2011.